Statistical Analysis Plan Amendment 4

Study ID: 213171

Official Title of the Study: A phase IIIB, randomized, controlled, observer-blind study to evaluate safety and immunogenicity of GSK's meningococcal ABCWY vaccine when administered in healthy adolescents and adults, previously primed with meningococcal ACWY vaccine.

NCT Number: NCT04707391

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STATISTICAL ANALYSIS PLAN

213171 (MENABCWY-019)

A phase IIIB, randomized, controlled, observer-blind study to evaluate safety and immunogenicity of GSK's meningococcal ABCWY vaccine when administered in healthy adolescents and adults, previously primed with meningococcal ACWY vaccine

AUTHOR: PPD

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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

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Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

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MODIFICATION HISTORY

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Final 1.0	24JUL2020	PPD	Not Applicable – First Version
Final 2.0	14OCT2020		Added APPENDIX 3 for details on protocol deviations and of exclusions from analysis sets
Final 3.0	05MAR2021		Updated this document based on the protocol amendment 2 dated 12Feb2021 Changes: Promoted one of the secondary endpoints to coprimary.
Final 4.0	10NOV2021		Change label of treatment groups in the TFLs Updated this document based on the protocol amendment 3 dated 01NOV2021 Changes: Include potential interim analysis. Include sensitivity analysis Use NHBA strain M13520
Final 5.0	05SEP2022		Adjust the visit windows for analysis Include information regarding IA process Updated APPENDIX 3 to match latest PDMP Medications coded using WHO-DD rather than GSK DD Update spelling mistakes in APPENDIX 3

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
AESI	Adverse event of special interest
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
BMI	Body mass index
BS	Blood sample
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CI	Confidence Interval
CSR	Clinical Study Report
eCRF	Electronic Case Report Form
ELISA	Enzyme-linked immunosorbent assay
ENR	Enrolled Set
EoS	End of Study
ES	Exposed Set
ESFU	Extended safety follow-up
EudraCT	European Union Drug Regulating Authorities Clinical Trials Database
FAS	Full Analysis Set
fHbp	Factor H binding protein
GMC	Geometric mean concentration
GMR	Geometric mean ratio
GMT	Geometric mean titer
GSD	Geometric standard deviation

Abbreviation	Definition
GSK	GlaxoSmithKline
hSBA	Human Serum Bactericidal Assay
ICH	International Council on Harmonisation
IgG	Immunoglobulin G
LAR	Legally acceptable representative
LL	Lower limit
LLOQ	Lower limit of quantitation
M	Month
mm	Millimeter
MAR	Missing at random
MCAR	Missing completely at random
MedDRA	Medical Dictionary for Regulatory Activities
MenABCWY	Meningococcal serogroups A, B, C, W, and Y investigational vaccine
MenACWY	Meningococcal serogroups A, C, W, and Y conjugate vaccine (Menveo)
MenB	meningococcal B (Bexsero)
NHBA	Neisseria heparin binding antigen
NI	Non-inferiority
PD	Protocol deviation
pIMD	Potential immune-mediated disease
PT	Preferred term
PPS	Per Protocol Set
ROW	Rest of the World
SAE	Serious adverse event
SAP	Statistical analysis plan

Abbreviation	Definition
SD	Standard deviation
SOC	System organ class
SSS	Solicited Safety Set
T	Telephone contact
USS	Unsolicited Safety Set
V	Visit
WHO	World Health Organisation

1. INTRODUCTION

This document describes the rules and conventions to be used in the presentation and analysis of immunogenicity and safety data for Protocol 213171 (MENABCWY-019). It describes the data to be summarized and analyzed, including specifics of the statistical analyses to be performed.

This statistical analysis plan (SAP) is based on protocol amendment 3.0, dated 01NOV2021.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. PRIMARY IMMUNOGENICITY OBJECTIVE

Immunological non-inferiority: MenABCWY vs. MenACWY (Family 1):
The first co-primary objective is to demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise (refer to Section 6.6) in human serum bactericidal assay (hSBA) titers against N. *meningitidis* serogroups A, C, W, and Y, at 1 month after the **second** MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).
Immunological non-inferiority: MenABCWY vs. MenACWY (Family 2):
The second co-primary objective is to demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise (refer to Section 6.6) in hSBA titers against *N. meningitidis* serogroups A, C, W, and Y, at 1 month after the **first** MenABCWY vaccination (0,6-months schedule) and 1 month after the MenACWY vaccination (single dose).

2.2. SECONDARY IMMUNOGENICITY OBJECTIVES

The secondary objectives are:

- To assess the immune response to MenABCWY (0,6-month schedule) and MenACWY

(single dose) vaccines against *N. meningitidis* serogroups A, C, W, and Y, at pre-vaccination (Day 1, Month 0) and 1 month after the **first and last** MenABCWY vaccinations and 1 month after the MenACWY vaccination.

- To assess the immune response to the MenABCWY vaccine (0,6-month schedule) against *N. meningitidis* serogroup B indicator strains, at pre-vaccination (Day 1, Month 0) at 1 month after the **last** MenABCWY vaccination.

Note: *N. meningitidis* serogroup B indicator strains include: (M14459 for factor H binding protein [fHbp] antigen, M13520 for NHBA antigen, 96217 for NadA antigen and NZ98/254 for PorA P1.4 antigen).

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2.4. PRIMARY SAFETY OBJECTIVE

The primary safety objective is to evaluate the safety and reactogenicity of the MenABCWY and MenACWY vaccines.

2.5. ENDPOINTS

The primary, secondary and tertiary endpoints to support regulatory decisions are described in the following sections.

2.5.1. PRIMARY IMMUNOGENICITY ENDPOINT

Immunological non-inferiority: MenABCWY vs. MenACWY (Family 1):
The first co-primary immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine, will be demonstrated if the lower limit (LL) of the 2-sided 95% CI for the group difference in percentages of participants in the PPS (as defined in Section 5.5) achieving a 4-fold rise (refer to Section 6.6) in hSBA titers is above −10%, for each serogroup, i.e., the percentages of participants with a 4-fold rise (refer to Section 6.6) in hSBA titers against N. meningitidis serogroups A, C, W, and Y at 1 month after the **second** vaccination for the ABCWY group (Day 211, Month 7), and 1 month after the single dose of MenACWY vaccination for the ACWY group (Day 31, Month 1), relative to baseline (Day 1, Month 0).

Immunological non-inferiority: MenABCWY vs. MenACWY (Family 2):
The second-co-primary immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine, will be demonstrated if the lower limit (LL) of the 2-sided 95% CI for the group difference in percentages of participants in the Per Protocol Analysis Set (PPS, as defined in Section 5.5) achieving a 4-fold rise (refer to Section 6.6) in hSBA titers is above −10%, for each serogroup, i.e., the percentages of participants with a 4-fold rise (refer to Section 6.6) in hSBA titers against *N. meningitidis* serogroups A, C, W, and Y at 1 month after the **first** vaccination for the ABCWY group (Day 31, Month 1), and 1 month after the single dose of MenACWY vaccination for the ACWY group (Day 31, Month 1), relative to baseline (Day 1, Month 0).

2.5.2. SECONDARY IMMUNOGENICITY ENDPOINTS

The immune response to MenABCWY (0,6-month schedule) and MenACWY (single dose) vaccines against *N. meningitidis* serogroups A, C, W, and Y, at pre-vaccination (Day 1, Month 0) and 1 month after the **first and last** MenABCWY vaccinations and 1 month after the single MenACWY vaccination will be demonstrated for participants in the Full Analysis Set (FAS, as defined in Section 5.4) by:

- The percentages of participants with hSBA titers ≥Lower Limit of Quantitation (LLOQ) against serogroups A, C, W, and Y:
  - at baseline (Day 1, Month 0) and at 1 month after the first (Day 31, Month 1) and the last vaccination (Day 211, Month 7) for the ABCWY group, and
  - at baseline (Day 1, Month 0) and 1 month after the single MenACWY vaccination for the ACWY group (Day 31, Month 1).
- The geometric mean titers (GMTs) against serogroups A, C, W, and Y:
  - at baseline (Day 1, Month 0) and at 1 month after the first (Day 31, Month 1) and the last (Day 211, Month 7) vaccinations for the ABCWY group, and
  - at baseline (Day 1, Month 0) and 1 month after the single MenACWY vaccination for the ACWY group (Day 31, Month 1).
- The geometric mean ratios (GMRs) against serogroups A, C, W, and Y:
  - at 1 month after the first (Day 31, Month 1) and the last vaccination (Day 211, Month 7) for the ABCWY group as compared to baseline (Day 1, Month 0) and
  - at 1 month after the MenACWY vaccination (Day 31, Month 1) for the ACWY group as compared to baseline (Day 1, Month 0).

The immune response to the MenABCWY vaccine (0,6-month schedule) against *N. meningitidis* serogroup B indicator strains, at pre-vaccination (Day 1, Month 0) and at 1 month after the **last** MenABCWY vaccination will be demonstrated for participants in the FAS (as defined in Section 5.4) from:

- The percentages of participants with hSBA titers ≥LLOQ for each and all serogroup B indicator strains at baseline (Day 1, Month 0) and at 1 month after the last vaccination (Day 211, Month 7) for the ABCWY group.

- The percentages of participants with 4-fold rise (refer to Section 6.6) in hSBA titers against each *N. meningitidis* serogroup B indicator strains at 1 month after the last vaccination (Day 211, Month 7) relative to baseline (Day 1, Month 0) for the ABCWY group.
- GMTs against each serogroup B indicator strains at baseline (Day 1, Month 0) and at 1 month after the last vaccination (Day 211, Month 7) for the ABCWY group.
- GMRs against each serogroup B indicator strains at 1 month after the last vaccination (Day 211, Month 7) as compared to the baseline (Day 1, Month 0) for the ABCWY group.

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ACWY group (Day 31, Month 1).

2.5.4. PRIMARY SAFETY ENDPOINTS

The safety and reactogenicity of the MenABCWY and MenACWY vaccines will be demonstrated for participants in the corresponding Safety Sets (as defined in Sections 0, 5.6.2 and 5.6.3) from:

- The frequencies and percentages of participants with solicited administration site events (i.e., injection site pain, erythema, swelling, induration) and solicited systemic events (i.e., fever [body temperature ≥38.0°C/100.4°F], nausea, fatigue, myalgia, arthralgia, headache) during the 7 days (including the day of vaccination) following vaccination at Day 1, Month 0 (for the ABCWY and ACWY groups) and Day 181, Month 6 (for the ABCWY group).
- The frequencies and percentages of participants with any unsolicited AEs (including all SAEs, AEs leading to withdrawal, AESIs and medically attended AEs) during the 30 days (including the day of vaccination) following vaccination at Day 1, Month 0 (for the ABCWY and ACWY groups) and Day 181, Month 6 (for the ABCWY group).
- The percentages of participants with SAEs, AEs leading to withdrawal, AESIs and medically attended AEs throughout the study period (Month 0 to Month 12).

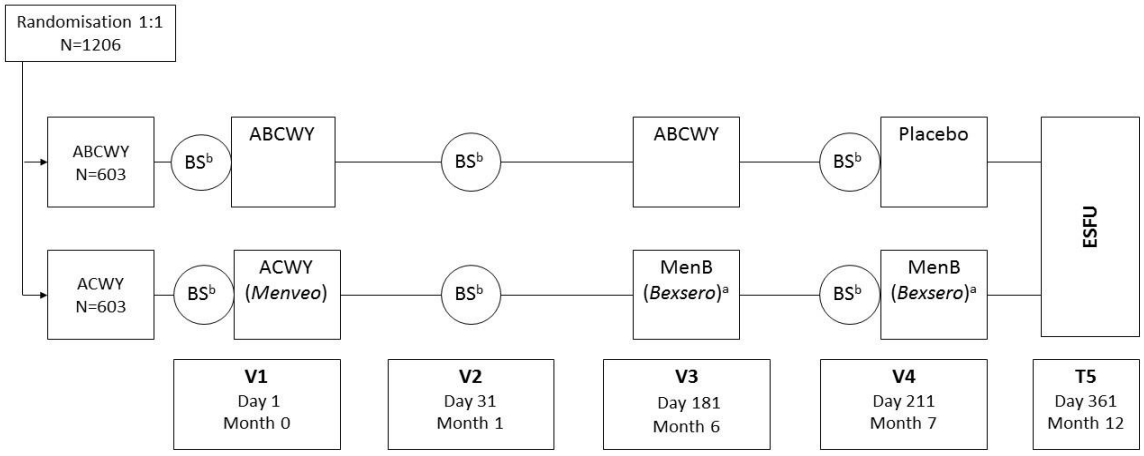
3. STUDY DESIGN

3.1. GENERAL DESCRIPTION

The study design diagram is provided in

Figure 1.

Figure 1 Study Design Overview



ACWY = *Menveo*; BS = blood sample; ESFU = extended safety follow-up; MenB = *Bexsero*; N = number of participants; T = telephone contact; V = visit

[a] *Bexsero* is given for compliance with standard of care

[b] Insufficient blood volume may lead to test cancellation and jeopardize the statistical power. Hence, every effort must be made to collect blood volume as per protocol requirements.

- Approximately 1206 participants will be randomized in a 1:1 ratio to achieve 1084 evaluable participants (at least 542 per group). Participants to receive:
  - **ABCWY:** At least 603 participants will receive 2 doses of the MenABCWY vaccine at

Visit 1 (Day 1) and Visit 3 (Day 181) (0,6-month schedule) and 1 dose of placebo at Visit 4 (Day 211).

- **ACWY:** At least 603 participants will receive 1 dose of MenACWY vaccine at Visit 1 (Day 1) (single dose) and 2 doses of MenB vaccine at Visit 3 (Day 181) and Visit 4 (Day 211).

Randomization will be minimized for country. Study vaccine groups, intervention and blinding foreseen in the study are presented in

Figure 1 and
Table 1. For further details please refer to Section 3.0 of the protocol.

Table 1 Study Vaccine Groups, Intervention, and Blinding Foreseen in the Study

Study Vaccine Group	Number of Participants	Age (Min to Max)	Intervention	Blinding
ABCWY	625	15 to 25 years	MenABCWY Placebo	V1 to T5: Observer-blind
ACWY	625	15 to 25 years	MenACWY MenB	V1 to T5: Observer-blind

MenACWY = *Menveo*; MenB = *Bexsero*; T = telephone contact; V = visit

3.2. SCHEDULE OF EVENTS

Schedule of events can be found in Section 1.3 of the protocol.

3.3. CHANGES TO ANALYSIS FROM PROTOCOL

The visit window in the protocol is -5/+14 days for visits 2, 3 and 4. For the statistical analysis this window will be -7/+28 days for each visit.
There are no other changes to planned analyses in the protocol. However, during special circumstances such as the COVID-19 pandemic, the specific guidance from local public health and other competent authorities regarding the protection of individuals' welfare will be applied. For the duration of such special circumstances, some measures may impact the data and analysis:

- Delayed FPI
- Protocol deviations due to COVID-19
- Missed visits due to COVID-19
- Missed or modified assessments
- Treatment interruptions or delays
- Early study discontinuation or withdrawals due to having COVID-19 or COVID-19 related issues
- Adverse events or SAEs due to COVID-19

The number and percentage of participants experiencing any of the COVID related consequences listed above will be presented.

4. PLANNED ANALYSES

The following analyses will be performed for this study:

- Interim analysis
- Final Analysis

4.1. DATA MONITORING COMMITTEE (DMC)

There will be no DMC for this study.

4.2. INTERIM ANALYSIS

An interim analysis of safety objectives will be conducted after at least 50% of participants have completed Visit 4. An interim analysis of immunological objectives may also be performed after all participants have completed Visit 4. If performed, the assessment of the primary immunological objectives will follow the order described in section 16.1.3 with analysis of family 1 preceding that of family 2.

The interim analysis will be performed by the unblinded analysis team who are independent of the blinded analysis team. Only unblinded analysis tables will be provided to avoid the reviewer being unblinded at a participant level.

4.3. FINAL ANALYSIS

All final, planned analyses identified in this SAP will be performed by IQVIA Biostatistics following GlaxoSmithKline authorization of this Statistical Analysis Plan, Database Lock, Sponsor Authorization of Analysis Sets and Unblinding of intervention.

5. ANALYSIS SETS

Agreement and authorization of participants included/excluded from each analysis set will be conducted prior to the unblinding of the study.

5.1. PROCESS FOR ANALYSIS SET ASSIGNMENT

- Preliminary analysis sets will be derived, prior to the database lock, to the extent that data is available.
- Data listings presenting participants excluded from each preliminary analysis set and reasons for exclusion will be prepared for sponsor review ahead of database lock (during the data review meeting) in order to allow appropriate related data queries to be issued.
- The final analysis sets will be derived after database lock and will use the final study data, i.e., clinical database (CRF), external vendor data (serological results), eDiaries and protocol

deviations log.

- Data listings presenting participants excluded from each final analysis set and reasons for exclusion will be prepared for sponsor review ahead of unblinding for a final review and approval.
- Customer authorization of the analysis sets will be necessary to unblind the data after database lock.

5.2. ENROLLED SET [ENR]

The enrolled set (ENR) will contain all participants who agreed/participants for whom parent(s)/legally acceptable representative agreed to participate in a clinical study after completion of the informed consent process, who meet screening/eligibility criteria and randomized or received study intervention or undergone an invasive procedure.

For analyses and displays based on ENR, participants will be classified according to randomized intervention.

5.3. EXPOSED SET [ES]

The exposed set (ES) will contain all participants who received at least 1 dose of the study intervention.

The allocation in a group is done according to all administered interventions. If there is any doubt whether a participant was vaccinated or not, they will be assumed vaccinated for the purposes of analysis. Participants will be classified according to intervention received.

5.4. FULL ANALYSIS SET [FAS]

The FAS will contain all participants who received at least 1 dose of the study intervention and have post-vaccination immunogenicity data, i.e., available hSBA titer for at least one serogroup (A, B, C, W or Y).

For analyses and displays based on the FAS, participants will be classified according to the randomized intervention.

Note: The intent-to-treat principle is preserved, despite the exclusion of participants randomized who did not receive the study intervention, because the decision of whether or not to begin the intervention could not be influenced by knowledge of the assigned intervention, i.e. the study medication is blinded.

5.5. PER PROTOCOL ANALYSIS SET [PPS]

The PPS will contain all participants who received at least 1 dose of the study intervention to which they are randomized and have post-vaccination data (FAS) minus participants with protocol deviations that lead to exclusion from the PPS, as defined prior to analysis.

5.6. SAFETY ANALYSIS SETS

In case of a vaccination error (wrong vaccine), participants will be analyzed as "treated" (i.e., according to the vaccine a participant receives, rather than the vaccine to which the participant is randomized).

5.6.1. UNSOLICITED SAFETY ANALYSIS SET [USS]

The unsolicited safety analysis set (USS) will contain all participants who received at least 1 dose of the study intervention (ES) that report unsolicited AEs/report not having unsolicited AEs.

5.6.2. SOLICITED SAFETY ANALYSIS SET [SSS]

The solicited safety analysis set (SSS) will contain all participants who received at least 1 dose of the study intervention (ES) who have solicited safety data.

5.6.3. OVERALL SAFETY ANALYSIS SET [OSS]

The overall safety analysis set (OSS) will contain all participants who are in the Solicited Safety Set and/or Unsolicited Safety Set.

5.7. OVERVIEW OF ANALYSIS BY PROTOCOL DEVIATION (PD)

Details of PDs can be found in the Protocol Deviation Management Plan and in APPENDIX 3 of this SAP.

6. GENERAL CONSIDERATIONS

Immunogenicity and safety endpoints will be summarized descriptively (frequency and percent for categorical data; and number of participants with non-missing observations, mean [or geometric mean], standard deviation [SD] [or geometric standard deviation {GSD}], median, minimum, and maximum for continuous data, unless specified otherwise) at all relevant study visits, as appropriate. In summary tables for categorical data for which categories are defined on the electronic case report form (eCRF), all categories will be presented as specified, even if the participant count within that category is zero.

Unless otherwise specified, all data collected during the trial will be presented in the data listings.

6.1. REFERENCE START DATE AND STUDY DAY

Study Day will be calculated from the reference start date and will be used to show start/stop day of assessments and events.

Reference start date is defined as the day of the first dose of study medication, (Day 1 is the day of the first vaccination).

- If the date of the event is on or after the reference date then:
  - Study Day = (date of event – reference date) + 1.

In the situation where the event date is partial or missing, Study Day, and any corresponding durations will appear partial or missing in the data listings.

6.2. BASELINE

Unless otherwise specified, baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments). In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-baseline, but Adverse Events (AEs)

and medications commencing on the reference start date will be considered post-baseline.

6.3. RETESTS, UNSCHEDULED VISITS AND EARLY TERMINATION DATA

Not applicable.

6.4. WINDOWING CONVENTIONS

The following table describes assignment of visit windows to the following data for purposes of the immunogenicity analysis:

Table 2 Visit Windows for Immunogenicity by Visit

Assigned Study Day (Inclusive)		**Visit Assigned**	**Day Assigned**	**Month Assigned**
From	**To**			
1 (pre-vaccination)	1 (pre-vaccination)	Visit 1	1	Baseline
24	59	Visit 2	31	Month 1
173	208	Visit 3	181	Month 6
24*	59*	Visit 4	Visit 3 + 31	Month 7

* Based on number of days from visit 3

6.5. STATISTICAL TESTS

The default significance level will be (5%); confidence intervals will be 95% and all tests will be two-sided, unless otherwise specified in the description of the analyses.

6.6. COMMON CALCULATIONS

Geometric Mean Titer/Concentration (GMT/GMC)

Distributions of antibodies are generally skewed to the right (Nauta, 2010). Therefore, prior to any statistical analysis that assumes normally distributed observations, antibody titers or concentrations will be $\log_{10}$-transformed. GMTs [/GMCs] and their 95% CIs are computed by exponentiating (base 10) of the $\log_{10}$ titers.

The GMT [/GMC] will be calculated using the following formula:

$$10^{\left(\frac{\sum_{i=1}^{n}\log 10(t_i)}{n}\right)}$$

Where $t_1, t_2, \ldots, t_n$ are n observed immunogenicity titers/concentrations.

Geometric Mean Ratio (GMR)

GMRs measure the changes in immunogenicity titers/concentrations *within* participants.
The GMR will be calculated using the following formula:

$$10^{\left(\frac{\sum_{i=1}^{n_g}\log 10\left({}^{v_{ij}}/_{v_{ik}}\right)}{n_g}\right)} = 10^{\left(\frac{\sum_{i=1}^{n_g} log10(v_{ij}) - log10(v_{ik})}{n_g}\right)}$$

where, for n_g participants in vaccine groups g =1 and 2, v_{ij} and v_{ik} are observed immunogenicity titers/concentrations for participant i at time-points j and k, j ≠ k.

4-fold rise

For the serogroups A, C, W, Y and for each of the serogroup B indicator strains evaluation the 4-fold rise is defined as:

- a post-vaccination hSBA titer ≥16 for participants with a pre-vaccination hSBA titer <4;
- a post-vaccination hSBA titer ≥4 times the LLOQ for participants with a pre vaccination hSBA titer ≥limit of detection (LOD) but <LLOQ; and,
- a post-vaccination hSBA titer ≥4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer ≥LLOQ.

6.7. SOFTWARE VERSION

All analyses will be conducted using SAS version 9.4 or higher.

7. STATISTICAL CONSIDERATIONS

7.1. ADJUSTMENTS FOR COVARIATES AND FACTORS TO BE INCLUDED IN ANALYSES

The following covariates and factors will be used in the analyses in addition to the vaccine group. For details of their inclusion in the models, see the specific analysis subsections in Section 16.

- Baseline titers as a covariate in the Analysis of Covariance (ANCOVA) models
- Country as a factor in the Analysis of Variance (ANOVA) and ANCOVA models.

7.2. MULTICENTER STUDIES

This study will be conducted by multiple investigators at multiple centers in approximately 4 countries. Randomization to vaccine group will be minimized by country. Additional analyses by country may be conducted as deemed necessary.

For continuous endpoints (GMT/GMR), the vaccine group effects will be investigated using a linear model that includes a factor for country differences but will not consider vaccine-by-country interaction, i.e., the model only considers effects for country and vaccine. If the statistical model does not converge due to the factor "country", a model without country effect will be fitted instead. If significant vaccine effects are found in a trial, there will be an exploration of the heterogeneity of vaccine group effects across countries. Results of vaccine by country interaction analysis will be provided in Appendix 16.1.9 of the Clinical Study Report (CSR).

7.3. MISSING DATA

There will only be limited imputation of missing data. To minimize the effect of dropouts and missing data, the study period will be divided into time intervals for statistical analysis of safety.

Unsolicited Adverse Events Missing or Partial Dates

Missing and partial AE start dates will be imputed as described in APPENDIX 2, only to determine the relationship between the start date of the event and the first dose date of vaccination. Partial dates will be presented as recorded in the data listings.

Missing intensity and relatedness for unsolicited AEs

Missing severity, relationship with study vaccine, and outcome of unsolicited adverse events will not be replaced and will appear as 'UNKNOWN' in all statistical output.

Missing Solicited Event Measurements

On the solicited events eDiary, participants are instructed to enter a measurement for solicited administration site events (i.e., injection site pain, erythema, swelling, induration) and solicited systemic events (i.e., fever [body temperature ≥38.0°C/100.4°F], nausea, fatigue, myalgia, arthralgia, headache) during the 7 days (including the day of vaccination) following vaccination at Day 1, Month 0 and Day 181, Month 6.

Titers Measured Below (or Above) the LLOQ (or ULOQ)

For the hSBA assay, a titer value measured below LLOQ will be imputed to a value that equal to LLOQ/2 in summaries and analyses but will be listed as reported in the raw serology data. For example, a serologic assay with LLOQ = 30 generally reports values below LLOQ as "<30". The data listings will present the values as "<30", while values of 15 are to be used in the summaries and analyses.

Titer values measured as above ULOQ will be imputed at the ULOQ value.

Otherwise, missing immunogenicity values are considered Missing Completely at Random (MCAR) and "therefore will not contain information that impact the result of the analysis (i.e., not informative). Imputation methods will therefore not be used.

7.4. MULTIPLE COMPARISONS/ MULTIPLICITY

For the multiplicity adjustment, all hypotheses will be ranked into two families, family 1 and family 2. Fixed sequential testing with full alpha propagation in these pre-ordered hypotheses families will be applied. Refer protocol section 9.2 sample size determination for more details.

7.5. ACTIVE-CONTROL STUDIES INTENDED TO SHOW NON-INFERIORITY

NI will be demonstrated if, the lower limit of 2-sided 95% confidence interval (CI) for the percent difference in 4-fold rise (refer to Section 6.6) in hSBA titers (p_MenABCWY- p_MenACWY) is above −10%, for each N. meningitidis A, C, W, and Y serogroup. Additional details provided in Section 16 of this SAP.

7.6. EXAMINATION OF SUBGROUPS

Subgroup analyses will be conducted for the Primary immunogenicity analyses only. It should be noted that the study was not designed to detect treatment differences with high statistical power within subgroups. The following subgroups will be assessed and described within the immunogenicity analysis sections: Gender (Female, Male), Race (White, Non-white), Age in years (15 to <18, ≥18-25), Country (by country, and 'US vs. Rest of the World (ROW)'.

7.7. RANDOMIZATION AND BLINDING

7.7.1. METHOD OF GROUP ASSIGNMENT AND RANDOMIZATION

For further details please refer to Section 6.3 of the protocol.

7.7.2. DEFINITION OF RANDOMIZATION/VACCINATION ERRORS

The list below provides some examples of potential errors that may occur during vaccination:

- Administration of concomitant vaccine(s) forbidden in the protocol (code 1040)
- Randomisation failure (participant not randomized in correct group) (code 1050)
- Randomisation code was broken (code 1060)

- Dosing not according to protocol (code 1070)
- Dosing after a Temperature deviation (code 1080)
- Dosing after expiration (code 1090)

Randomization errors will be summarized by presenting the number and percentage of participants with randomization errors for the enrolled set. Participants with randomization errors should be analyzed as randomized in FAS, excluded from PPS and analyzed as received for Safety.

8. OUTPUT PRESENTATIONS

Programming Conventions for Outputs shows conventions for presentation of data in outputs.

The templates (table shells) provided with this SAP describe the presentations for this study and therefore the format and content of the summary tables, figures, and data listings to be provided by IQVIA Biostatistics.

Statistical output numbering will follow 'ICH E3 Structure and Content of Clinical Study Reports'.

9. DISPOSITION AND WITHDRAWALS

All participants from the ENR Set will be accounted for in this study.

9.1. DISPOSITION

The number of enrolled, vaccinated (at least 1 vaccination, full vaccination course), completed participants, screening failures, reason for withdrawal, and reason for exclusion from analysis sets, as well as number of participants in FAS and PPS will be reported by group for the ENR set. Additionally, the number of participants discontinuing the study and the reason for discontinuation, including COVID-19, will be presented.

A data listing of the disposition information will be provided. If applicable, early study discontinuation or withdrawals due to having COVID-19 or COVID-19 related issues will be presented. The number of

participants who discontinued study drug and who withdrew from the Study due to COVID-19 infection or issues related to the COVID-19 pandemic will be presented.

9.2. PROTOCOL DEVIATIONS

Protocol deviations will be collected in a PD log, as detailed in the Protocol Deviations Management Plan.

All protocol deviations will be assessed as important or non-important. Protocol deviations will be reviewed by the GSK Team, and their status confirmed by the time that all data are cleaned for the Final Analysis. APPENDIX 3 lists PDs that affect the validity of the immunogenicity measurements and result in exclusion of participants from the PPS.

A summary presenting the number and percentage of participants in each PD category will be presented for participants in the ENR set, by vaccine group and overall, and a data listing will be provided for participants with protocol deviations during the study. Additionally, a data listing of PDs for participants who are excluded from the PPS will be generated.

A summary presenting the number and percentage of participants with a protocol deviation related to COVID-19 in each PD category will be presented for participants in the ENR set, by vaccine group and overall. Additionally, PDs related to COVID-19 will be flagged in the PD listing.

10. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic data and other baseline characteristics will be presented for the ENR, ES, FAS and PPS. No statistical testing will be carried out for demographic or other baseline characteristics.

The following demographic and other baseline characteristics will be reported for this study: Age (years) at the time of the first vaccination, Sex, Race, Ethnicity, Weight (kg), Height (cm) and Body Mass Index (BMI) (kg/m^2). Descriptive statistics (mean, standard deviation [SD], median, minimum and maximum) for age, height, weight, and body mass index will be calculated overall and by vaccine group. Distributions of participants by sex, race, and ethnic origin will be summarized overall and by vaccine group.

10.1. DERIVATIONS

Age (years) at first vaccination

When age at vaccination is to be displayed in years, it will be calculated as the number of complete calendar years between the date of birth and the date of vaccination. For example:

- DOB = 10SEP1983, Date of vaccination = 09SEP2018 -> Age = 34 years
- DOB = 10SEP1983, Date of vaccination = 10SEP2018 -> Age = 35 years

Note: If we have partial DOB, the DOB will be imputed as described in APPENDIX 2.

Weight

Weight will be presented in kilograms. Weights reported in pounds will be converted as follows:

- Weight in kilograms = Weight in pounds / 2.2

Height

Height will be presented in centimeters. Heights reported in feet and inches will be converted as follows:

- Height in centimeters = Height in inches x 2.54

Body mass index (BMI)

BMI will be calculated as follows:

- BMI (kg/ m^2)= (Weight in kilograms) / (Height in meters)^2

Temperature

Temperatures will be presented in degrees Celsius (°C). Temperatures reported in degrees Fahrenheit (°F) will be converted as follows:

- Temperature (Celsius) = ((Temperature (Fahrenheit) - 32) x 5)/9

11. VACCINATION AND MEDICAL HISTORY

Vaccination and Medical History information will be presented for the ES.

- Vaccination History:
  - Identity of the primary MenACWY vaccination
  - Age at primary MenACWY vaccination.
- Medical History will be coded using the current version of the Medical Dictionary for Regulatory Activities (MedDRA):
  - Medical History conditions are defined as those conditions which stop prior to or at the first vaccination.
  - Presented by System Organ Class (SOC) and Preferred term (PT).

12. CONCOMITANT ILLNESSES

Concomitant Illnesses (also captured on the Medical History page) will be presented for the ES.

- Concomitant Illnesses will be coded using the current version of the MedDRA dictionary:
  - Concomitant Illnesses are conditions which started prior to the first vaccination and are ongoing at the first vaccination.
  - Presented by SOC and PT.

13. MEDICATIONS

Medications will be presented for the ES and coded using the current version of World Health Organization (WHO) Drug dictionary. Medications will be presented by anatomical therapeutic chemical (ATC) classification and preferred drug name, overall and by vaccine group.

See APPENDIX 2 for handling of partial dates for medications, in the case where it is not possible to define a medication as prior or concomitant, the medication will be classified by the worst case; i.e. concomitant.

- 'Prior' medications are medications which started and stopped prior to the first vaccination.
- 'Concomitant' medications are medications which:
  - started prior to, on or after the first vaccination, AND

- ended on or after the date of first vaccination or were ongoing at the end of the study.

14. STUDY MEDICATION EXPOSURE

The total time in the study (including follow-up after the last vaccination) will be summarized as a continuous variable by vaccine group and overall. The total time in study is defined as the number of days from the first vaccination to the date of last contact specified on the End of Study Visits form. This will generally be the date of the last telephone contact (scheduled on Day 361). The vaccination date/time information will be listed for each participant.

14.1. DERIVATIONS

Total time in study (days) = date of last contact – date of first vaccination + 1.

15. STUDY MEDICATION COMPLIANCE

Compliance to study medication will be presented for the ES.
The number and percentage of participants receiving 1 dose, 2 doses or all 3 doses will be presented overall and by vaccine group for the ES. For each intervention, the number of participants receiving the vaccine outside the specified window will be presented.

The number and percentage of participants who missed each dose or received the dose outside the planned window due to COVID-19 will be presented (if applicable) overall and by vaccine group for the ES.

16. IMMUNOGENICITY OUTCOMES

16.1. PRIMARY IMMUNOGENICITY

16.1.1. PRIMARY IMMUNOGENICITY VARIABLE & DERIVATIONS

The first co-primary immunogenicity variable is the percentages of participants with a 4-fold rise (refer to

Section 6.6) in hSBA titers against N. meningitidis serogroups A, C, W, and Y at 1 month after the **second** vaccination for the ABCWY group (Day 31, Month 1), and 1 month after the single dose of MenACWY vaccination for the ACWY group (Day 31, Month 1), relative to baseline (Day 1, Month 0).

The second co-primary immunogenicity variable is the percentages of participants with a 4-fold rise (refer to Section 6.6) in hSBA titers against N. meningitidis serogroups A, C, W, and Y at 1 month after the **first** vaccination for the ABCWY group (Day 31, Month 1), and 1 month after the single dose of MenACWY vaccination for the ACWY group (Day 31, Month 1), relative to baseline (Day 1, Month 0).

16.1.2. MISSING DATA METHODS FOR PRIMARY IMMUNOGENICITY VARIABLE(S)

Refer to Section 7.3.

16.1.3. PRIMARY ANALYSIS OF PRIMARY IMMONOGENICITY VARIABLE

The following study hypotheses are ordered into 2 families that will be tested in sequential design with full alpha propagation. Family 1 will be tested first and family 2 will only be tested if the hypothesis in family one is successfully demonstrated.

First Co-Primary Immunogenicity Objective (Family 1):
The first co-primary immunogenicity objective is to demonstrate the immunological non-inferiority of the antibody response to MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with MenACWY, as measured by percentage of participants with 4-fold rise (refer to Section 6.6) in hSBA titer against each of the *N. meningitidis* serogroups A, C, W, and Y, at 1 month after the **second** MenABCWY vaccination and 1 month after the MenACWY vaccination (single dose). This translates to the following hypotheses:

H_0: $(p1\_MenABCWY_{(i)} - p1\_MenACWY_{(i)}) \leq -10\%$

vs.

H_1: $(p1\_MenABCWY_{(i)} - p1\_MenACWY_{(i)}) > -10\%$

Where p1_MenABCWY$_{(i)}$ denotes the percentages of participants with 4-fold rise (refer to Section 6.6) in hSBA titers for serogroups i=A, C, W, and Y, 1 month after the **second** vaccination of MenABCWY group and p1_MenACWY$_{(i)}$ denotes the percentages of participants with 4-fold rise (refer to Section 6.6) in hSBA titers for serogroups i=A, C, W, and Y, 1 month after the single vaccination of MenACWY group.

The primary immunogenicity analysis will be performed for the PPS. The primary immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine, will be demonstrated if the lower limit (LL) of the 2-sided 95% CI for the group difference in percentages of participants achieving a 4-fold rise (refer to Section 6.6) in hSBA titers is above −10%, for each serogroup.

For each of the serogroups A, C, W, Y the percentages of participants with 4-fold rise (refer to Section 6.6), and the corresponding exact 2-sided 95% CIs based on Clopper-Pearson method (Clopper and Pearson, 1934) will be calculated for each vaccine group at 1 month post **second** vaccination. The standardized asymptotic CIs between group differences in percentages will be derived using the method of Miettinen and Nurminen (Nurminen, 1985).

Second Co-Primary Immunogenicity Objective (Family 2):
The second co- primary immunogenicity objective is to demonstrate the immunological NI of the antibody response to MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with MenACWY, as measured by percentage of participants with 4-fold rise (refer to Section 6.6) in hSBA titer against each of the *N. meningitidis* serogroups A, C, W, and Y, at 1 month after the **first** MenABCWY vaccination and 1 month after the MenACWY vaccination (single dose). This translates to the following hypotheses:

H_0: $(p2\_MenABCWY_{(i)} - p2\_MenACWY_{(i)}) \leq -10\%$

vs.

H_1: $(p2\_MenABCWY_{(i)} - p2\_MenACWY_{(i)}) > -10\%$

Where p2_MenABCWY$_{(i)}$ denotes the percentages of participants with 4-fold rise (refer to Section 6.6) in hSBA titers for serogroups i=A, C, W, and Y, 1 month after the **first** vaccination of MenABCWY group

and p2_MenACWY$_{(i)}$ denotes the percentages of participants with 4-fold rise (refer to Section 6.6) in hSBA titers for serogroups i=A, C, W, and Y, 1 month after the single vaccination of MenACWY group.

The secondary immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine, will be demonstrated if the lower limit (LL) of the 2-sided 95% CI for the group difference in percentages of participants achieving a 4-fold rise (refer to Section 6.6) in hSBA titers is above −10%, for each serogroup

For each of the serogroups A, C, W, Y the percentages of participants with 4-fold rise (refer to Section 6.6), and the corresponding exact 2-sided 95% CIs based on Clopper-Pearson method (Clopper, 1934) will be calculated for each vaccine group, at 1 month after the **first** vaccination for the ABCWY group (Day 211, Month 7), and 1 month after the single dose of MenACWY vaccination for the ACWY group (Day 31, Month 1). The standardized asymptotic CIs between group differences in percentages will be derived using the method of Miettinen and Nurminen (Nurminen, 1985). The secondary immunological non-inferiority analysis will be performed for the PPS.

16.1.4. Sensitivity Analysis of Primary Immunogenicity Variable(s)

Each co-primary immunogenicity objective will be analysed as a sensitivity analysis using a logistic regression with margins calculated by Taylors approximation with the minimization factors as covariables.

16.1.5. Subgroup Analysis of Primary Immunogenicity Variable(s)

The primary immunogenicity variables will be analysed for subgroups listed in Section 7.6

16.2. Secondary Immunogenicity

The secondary immunogenicity analyses will be performed for the FAS.

16.2.1. Secondary Immunogenicity Variables & Derivations

16.2.1.1. Immune Response, Serogroups A, C, W and Y (measured by hSBA)

The immune response to MenABCWY (0,6-month schedule) and MenACWY (single dose) vaccines against *N. meningitidis* serogroups A, C, W, and Y, at pre-vaccination (Day 1, Month 0) and 1 month after the **first and last** MenABCWY vaccinations and 1 month after the single MenACWY vaccination will be demonstrated using:

- Logarithmically transformed (base 10) hSBA titers and percentages of participants with hSBA titers ≥LLOQ:
    - at baseline (Day 1, Month 0) and at 1 month after the first (Day 31, Month 1) and the last vaccination (Day 211, Month 7) for the ABCWY group, and
    - at baseline (Day 1, Month 0) and 1 month after the single MenACWY vaccination for the ACWY group (Day 31, Month 1).

16.2.1.2. Immune Response, Serogroup B Indicator Strains (measured by hSBA)

The immune response to the MenABCWY vaccine (0,6-month schedule) against *N. meningitidis* serogroup B indicator strains:

- **M14459** for factor H binding protein [fHbp] antigen
- **M13520** for NHBA antigen
- **96217** for Nad A antigen; and
- **NZ98/254** for PorA P1.4 antigen

will be demonstrated using:

- Logarithmically transformed (base 10) hSBA titers
- The percentages of participants with hSBA titers ≥LLOQ for each and all serogroup B indicator strains at baseline (Day 1, Month 0) and at 1 month after the last vaccination (Day 211, Month 7) for the ABCWY group. For the 'all' serogroup B indicator strains to be considered as satisfying the '≥LLOQ' criteria, all 4 of the serogroup indicator strains hSBA titers must be ≥LLOQ.
- The percentages of participants with 4-fold rise (refer to Section 6.6) in hSBA titers against each *N. meningitidis* serogroup B indicator strains at 1 month after the last vaccination (Day 211, Month 7) relative to baseline (Day 1, Month 0) for the ABCWY group.

16.2.2. MISSING DATA METHODS FOR SECONDARY IMMONOGENICITY VARIABLES

Refer to Section 7.3

16.2.3. ANALYSIS OF SECONDARY IMMUNOGENICITY VARIABLES

16.2.3.1. Immune Response Analysis, Serogroups A, C, W and Y (measured by hSBA)

For each of the 4 *N. meningitidis* serogroups A, C, W, and Y the percentages of participants with hSBA titers ≥LLOQ and the corresponding exact 2-sided 95% CIs based on Clopper-Pearson method (Clopper) will be calculated at baseline (Day 1, Month 0), and at 1 month after the **first** (Day 31, Month 1) and the **last** vaccination (Day 211, Month 7) for the ABCWY group, and at baseline (Day 1, Month 0) and 1 month after the single MenACWY vaccination for the ACWY group (Day 31, Month 1).

The titers at baseline (Day 1, Month 0), at 1 month after the **first** (Day 31, Month 1) and the **last** vaccination (Day 211, Month 7) for the ABCWY group, and at 1 month after the single MenACWY vaccination (Day 31, Month 1) in the ACWY group, will be logarithmically transformed (base 10) to fulfill the normal distribution assumption.

GMTs and 95% CIs will be calculated by exponentiating (base 10) the least squares means and the lower and upper limits of the 95% CIs of the log-transformed titers (base 10) obtained from:

- an ANOVA with factors for vaccine group and country.
- an ANCOVA with baseline titers as a covariate, and factors for vaccine group and country.

GMRs (post vaccination/baseline titer) and associated 2-sided 95% CIs will be computed for each group and for each serogroup at each visit. GMRs will be calculated by exponentiating (base 10) the least squares means and the lower and upper limits of the 95% CIs of the log-transformed titers (base 10) obtained from an ANOVA with factors for vaccine group and country.

Additionally, GMTs and GMRs group ratios between the 2 vaccine groups and their respective 95% CIs will be computed by exponentiating the difference of the least square means of the log-transformed titers and the lower and upper limits of the 95% CIs on the difference obtained from the ANOVA model above.

16.2.3.2. Immune Response Analysis, Serogroup B Indicator Strains (measured by hSBA)

For *N. meningitidis* B indicator strains (M14459 for factor H binding protein [fHbp] antigen, M13520 for NHBA antigen, 96217 for NadA antigen and NZ98/254 for PorA P1.4 antigen):

- the percentages of participants with hSBA titers ≥LLOQ for each and all serogroup B indicator strains, and the corresponding exact 2-sided 95% CIs based on Clopper-Pearson method (Clopper) will be calculated for the MenABCWY vaccine group at at baseline (Day 1, Month 0), and at 1 month after the **last** vaccination (Day 211, Month 7).;and
- the percentage of participants with 4-fold rise (refer to Section 6.6) relative to baseline for each serogroup B indicator strains, and the corresponding exact 2-sided 95% CIs based on Clopper-Pearson method (Clopper) will be calculated for the MenABCWY vaccine group at at 1 month after the **last** vaccination (Day 211, Month 7).

GMTs and associated 2-sided 95% CIs will be computed for each serogroup B indicator strain at baseline (Day 1, Month 0), and at 1 month after the **last** vaccination (Day 211, Month 7) for the ABCWY vaccine group. The hSBA titers at baseline (Day 1, Month 0), and the hSBA titers at 1 month after the last vaccination (Day 211, Month 7) for the ABCWY group, will be logarithmically transformed (base 10) to fulfill the normal distribution assumption. For each *N. meningitidis* B test strain (M14459, M13520, 96217 and NZ98/254), the GMTs pre- and post-vaccination with their 95% CIs will be calculated by exponentiating (base 10) the means and the lower and upper limits of the 95% CIs of the log-transformed titers (base 10) values.

GMRs (post-vaccination/baseline titer) and associated 2-sided 95% CIs will be computed for each serogroup B indicator strain at 1 month after the **last** vaccination (Day 211, Month 7) for the ABCWY vaccine group, by exponentiating the corresponding log-transformed mean and 95% CI.

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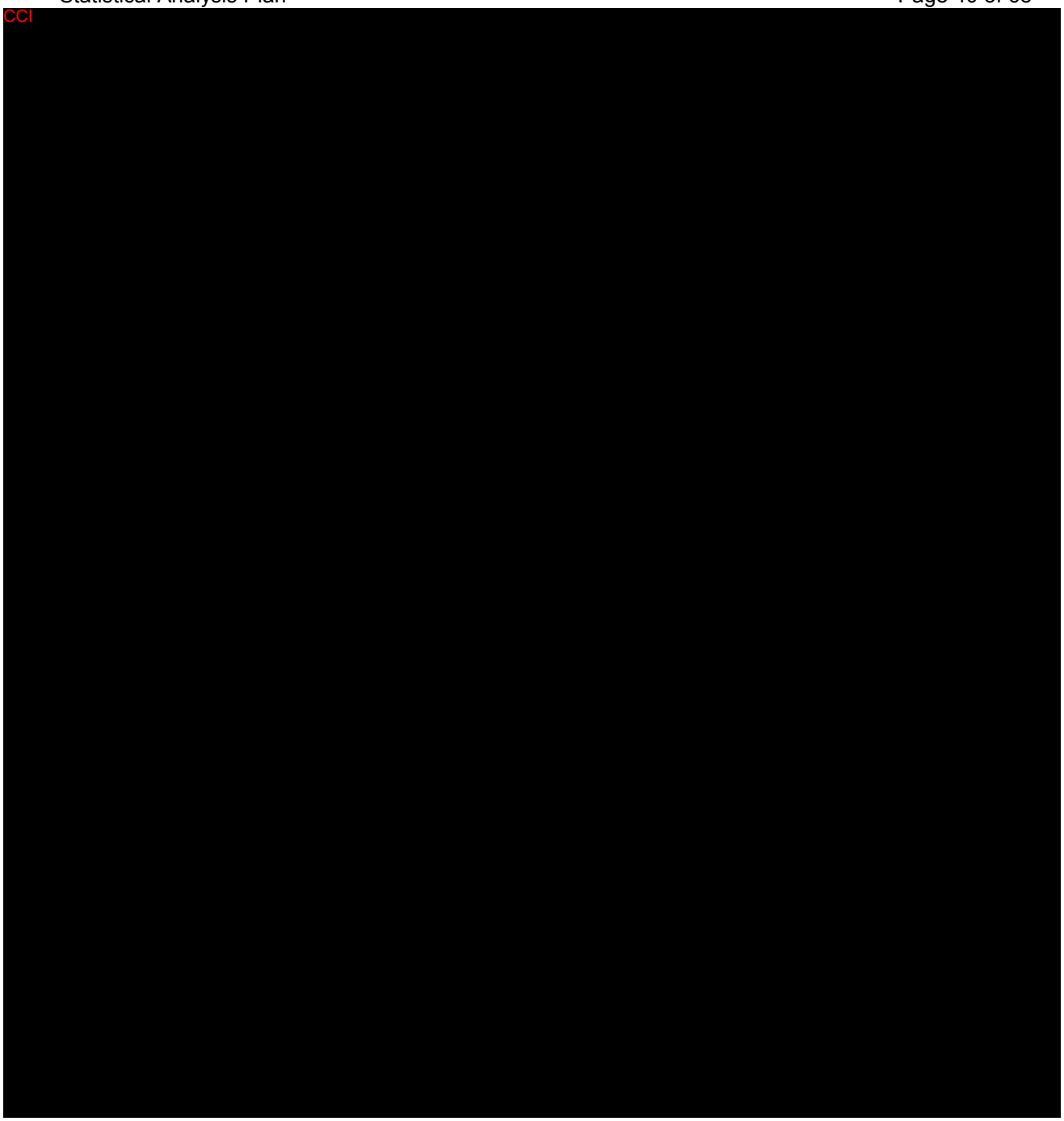

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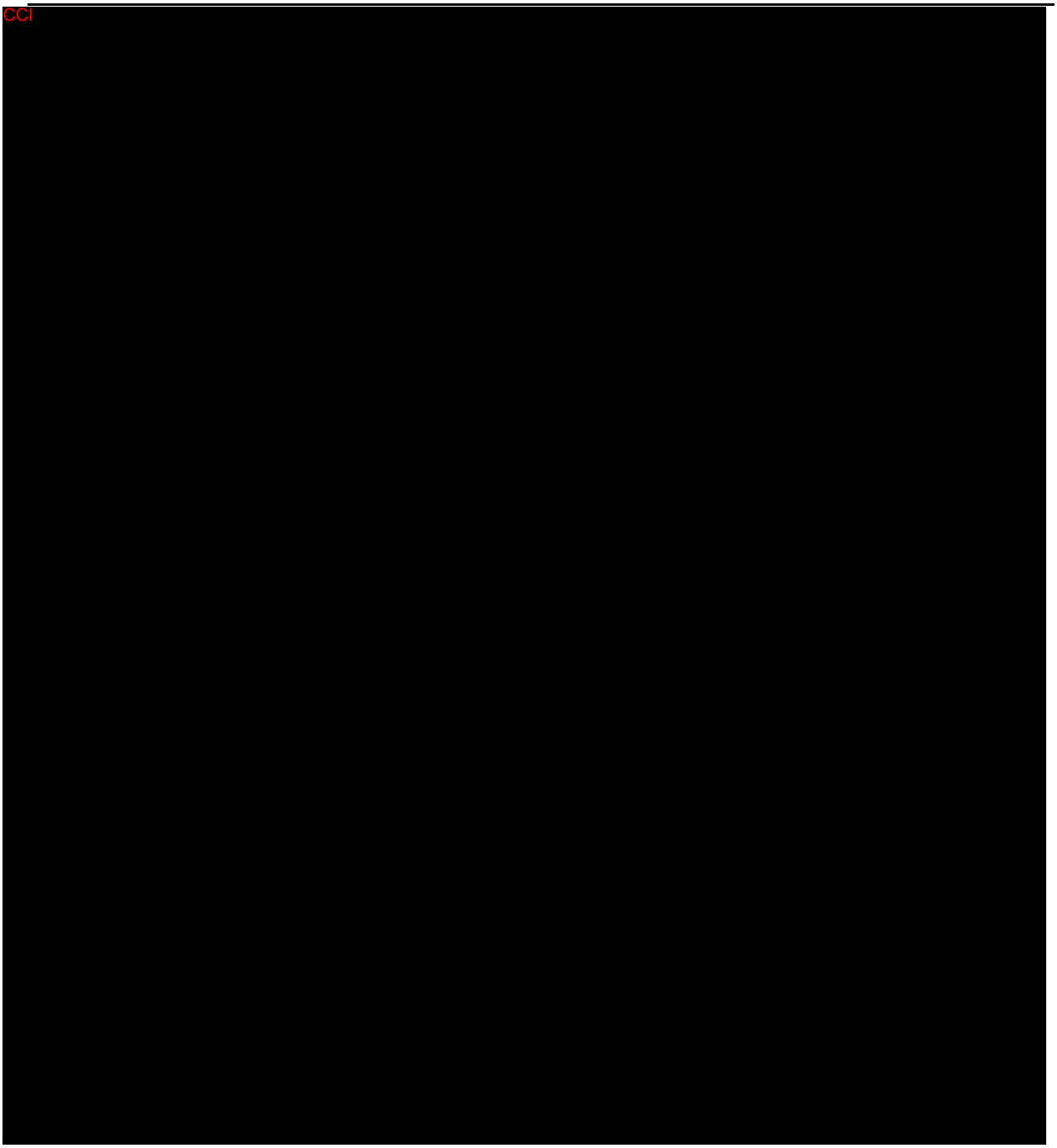

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17. SAFETY OUTCOMES

The analysis of safety assessments in this study will include summaries of the following categories of safety data collected for each participant:

- Solicited administration site and systemic adverse events and indicators of solicited events.
- Unsolicited adverse events.

There will be no statistical comparisons between the vaccine groups for safety data, unless otherwise specified with the relevant section.

17.1. ADVERSE EVENTS

Adverse Events (AEs) will be coded using the current version of the MedDRA dictionary.

See APPENDIX 2 for handling of partial dates for AEs. In the case where it is not possible to determine if an AE started after the first vaccination or not, the AE will be considered to have started after the vaccination.

17.1.1. SAFETY COMPLETENESS ANALYSIS

Solicited events (solicited administration site events and solicited systemic events)

The safety completeness analysis on solicited events aims to identify participants who completed the eDiary, irrespective of severity. The analysis will show the number of participants with valid data by solicited event, for each vaccination.

Four summaries will be produced:

- The frequencies of participants who provide eDiary information by vaccine group.
- For each solicited event, the frequencies of participants with valid data will be presented by vaccine group and time point: Day 1, Days 2, 3, 4, 5, 6 and 7.
- For each type of solicited event (administration site, systemic), the frequencies of participants with valid data by vaccine group, aggregated over time points: Day 1 - Day 7.
- For each solicited event, the frequencies of participants with valid data by vaccine group, aggregated over time points: Day 1 - Day 7.

For the corresponding percentages, the denominator will be the respective numbers of exposed participants, i.e., participants who received a vaccination and were still in-study for that time point or time interval, irrespective of whether an eDiary was available or not. All analyses will be based on the ES.

17.1.2. SOLICITED EVENTS

For details please refer to Appendix 4 of the protocol. Solicited events will be summarized using the SSS.

Only solicited administration site (i.e., injection site pain, erythema, swelling, induration) and systemic (i.e., fever [temperature ≥38.0°C/100.4°F], nausea, fatigue, myalgia, arthralgia, headache) adverse events reported in the diary card will be analyzed.

Solicited events will be reported daily starting on Day 1 and until Day 7 after each vaccination a Day 1 and Day 181 using structured eDiaries, i.e. Day 1 to Day 7 and Day 181 to 187. The analyses of solicited events will be done based on three intervals after each vaccination: Day 1 - 3, Day 4 - 7 and Day 1 - Day 7. Solicited site administration or systemic adverse events extending beyond 7 days will be presented separately. In addition:

- A solicited administration site or systemic adverse event ongoing after 7 days following each vaccination; or
- A solicited administration site or systemic adverse event that leads to a visit to a healthcare provider (medically attended AE); or
- A solicited administration site or systemic adverse event leading to the participant withdrawing from the study or the participant being withdrawn from the study by the investigator (AE leading to withdrawal); or
- A solicited administration site or systemic adverse event that otherwise meets the definition of an SAE
- Will be recorded and presented as an unsolicited AE.

For erythema, swelling and induration, recorded originally as diameters (mm), the following categorization will be used to summarize the data:

- None (< 25 mm) vs. any (>= 25 mm)
- None (< 25 mm), Mild (25-50 mm), Moderate (51-100 mm) and Severe (>100 mm)

Body temperature will be broken down by route of measurement according to the recommendations of the Brighton collaboration (www.brightoncollaboration.org) and will be summarized according to the 3 schemes described below:

- by 1.0 °C increments:
  - <36.0,
  - 36.0 - 36.9
  - 37.0 - 37.9

- 38.0 - 38.9
- 39.0 - 39.9
- ≥40.0°

- <38.0, ≥38.0 °C (i.e., 'no fever' versus 'fever')

Fever, defined as a body temperature of ≥38°C irrespective of route of measurement, will be integrated to the summaries as a systemic AE.

The analyses will encompass summaries of the data on five levels:

1. Daily reports of participants with solicited events.
2. Time of first onset of solicited events.
3. Solicited events, maximum event severity (i.e., severity grading scale as defined in Appendix 4 of the protocol) by event and interval Day 1 - 3, Day 4 - 7, and Day 1 – 7.
4. Duration of solicited events, excluding ongoing solicited events after Day 7.
5. Solicited events and indicators of solicited events, occurrence of at least one event by category (administration site, systemic) and interval Day 1 - 3, Day 4 – 7, Day 1 – 7 and extending beyond Day 7.

For studies using electronic diaries for the collection of solicited vents, a solicited event will be considered present only when a daily recording of grade 1 or more is present. For each of the time points or time intervals presented in the summaries, only participants with at least one observation for the solicited events in the interval of interest will be considered.

The analysis of solicited events after first vaccination will be reported separately from the analyses of solicited events after second vaccination. When the occurrences of solicited events are summarized, each event recorded as having occurred during a specific period will be counted as only one occurrence regardless of the number of days on which it occurs

Level 1: Daily reports of solicited events

For each of the time points, only participants with at least one observation for the solicited events in the

interval of interest will be considered. Data collected will be summarized (frequencies and percentages of participants) by vaccine group, solicited events, vaccination number and time point.

Level 2: Time of first onset of solicited events

The time of first onset is defined, for each participant, for each solicited event, as the time point at which the respective solicited event first occurred. For erythema, swelling and induration the following threshold will be used ≥ 25 mm. The summary will provide the frequencies and percentages of participants with first onset of each solicited events by vaccine group and vaccination number, and by each time point.
For each vaccination the first onset of the AE will be used for each participant. For any vaccination the worst AE across all vaccinations per time point will be used. Note, 'not done' is treated identical to 'missing'.

Level 3: Solicited events, maximum event severity by event and interval

The maximum event severity will be defined if there is at least one non-missing observation within this time interval, each participant's data will be aggregated across the time points of the interval and summarized according to the maximal severity observed for each adverse event, followed by a summary across participants for each vaccine group and vaccination. Participants without any solicited events in the interval, i.e., missing values at each of the requested time points, will be removed from the denominator.

Level 4: Number of days with solicited events

The duration of an event with a start and end date will be the number of days between the start and end dates plus one day, i.e. an event that starts on 03MAR2018 and ends on 12MAR2018 has a duration of 10 days.

The number of days with the AE is defined irrespective of severity. This means at least 'mild' solicited events that are assessed qualitatively ≥ 25, mm for erythema, swelling and induration. If a solicited event continues beyond Day 7 the period after Day 7 is not added.

The frequency distribution of the number of days will be provided in a summary table by vaccine group and vaccination, and by AE.

Level 5: Solicited events, occurrence of at least one event by category (administration site, systemic) and interval.

The occurrence of at least one solicited event is defined as "any" for a participant if he/she reports greater than "none" ≥ 25 mm, for erythema, swelling and induration for the respective event and "none" otherwise. The occurrence of at least one solicited event (i.e., none versus any) will be summarized by category (i.e., administration site, systemic, any), by vaccine group, by vaccination (after each vaccination and after any vaccination) and by time interval.

Use of antipyretics and analgesics to treat or prevent pain or fever will be summarized by frequencies and percentages of participants reporting use of the medications by type of use (prophylactic versus treatment) and for Day 1 - Day 3, Day 4 - 7, Day 1 - Day 7.

17.1.3. UNSOLICITED ADVERSE EVENTS

The unsolicited AEs will be summarized per the USS.

All the unsolicited AEs occurring during the study, judged either as probably related, possibly related, or not related to vaccination by the investigator, will be recorded. The original verbatim terms used by investigators to identify adverse events in the CRFs will be mapped to preferred terms using the MedDRA dictionary. The unsolicited AEs will then be grouped by MedDRA preferred terms into frequency tables according to system organ class. AEs judged by the investigator as at least possibly related to study vaccine will be summarized by vaccine group, according to system organ class and preferred term within system organ class. When an unsolicited AE occurs more than once for a participant, the maximal severity and strongest relationship to the vaccine group will be counted.

The dose relative to an event is the most recent study dose given to a participant prior to the start of a given event. For example, if the start date of an adverse event is between the first vaccination and the second vaccination, the relative dose will be the first vaccination.

If an event starts on the same day as a study dose, the relative dose will be derived from the additional information provided in the CRF using the contents of the flag indicating if the event occurred before or after vaccination. If 'after vaccination' is selected, the relative dose for the event will be the one administered on the start day of the event. If 'before vaccination' is selected, the relative dose for the event will be the dose prior to this one.

If an adverse event start date is missing or unknown, the AE will be considered as to have started after the first vaccination. For partially available dates, refer to APPENDIX 2.

Only adverse events with a start date on or after the first vaccination will be analyzed, i.e., excluding those after a participant has given informed consent but before the first vaccination. The selection of unsolicited AEs and the assignment to time intervals will be done by day of onset and not by days ongoing/persisting. AEs starting prior to the first vaccination, if any, will only be listed.

For each of the following intervals any unsolicited AE will be summarized:

- after each vaccination (from Day 1 to Day 31 and from Day 181 to Day 211, separately)
- after any vaccination (Day 1-31 and Day 181-211):
- entire study (Day 1 to end of study)

The following unsolicited adverse events will be summarized during the entire study:

- Possibly or probably related unsolicited AEs.
- Unsolicited AEs leading to death will be listed.
- Serious adverse events (SAEs).
- Possibly or probably related SAE.
- Possibly or probably related SAE leading to death
- Unsolicited AEs leading to premature withdrawal from study.
- Unsolicited AEs leading to discontinuation or delay in study vaccination.
- Unsolicited adverse events of special interest (AESI), as recorded on the Expedited AE report.
- Medically attended AEs.

Note: All the information required for the unsolicited AE summaries, including AESIs and medically attended AEs will be collected on the eCRF AE Form. Solicited events starting more than 7 days after the vaccination will also be considered as unsolicited AEs.

17.1.4. COMBINED SOLICITED AND UNSOLICITED ADVERSE EVENTS

A summary of participants with all combined solicited events (regardless of their duration; where erythema, swelling and induration are reported as any events with a diameter >= 1 mm) and unsolicited AEs will be provided. Unsolicited events will be coded by MedDRA. For clintrial.gov and EudraCT posting purposes, a summary of combined solicited and unsolicited non-SAEs will be produced by System Organ Class and according to occurrence of each event. For output combining solicited and unsolicited adverse events, all serious adverse events will be considered general events since the administration site flag is not included in the expedited adverse event CRF pages. Multiple events with the same preferred term which start on the same day are counted as only one occurrence. A further differentiation of combined AEs according to seriousness, severity, or relationship is not performed.

17.1.5. COVID-19 EVENTS

For the duration of special circumstances such as the COVID-19 pandemic, additional specific information will be summarized for the exposed set by vaccine group:

- Number of participants suspected, probable or confirmed for COVID-19 infection across diagnosis,
- Number of participants who had a COVID-19 diagnosis test and assessment performed
- Number of participants with positive, negative, or indeterminate results
- Incidence of COVID-19 reported as an adverse event or serious adverse event,
- Incidence of treatment discontinuation due to adverse event of COVID-19 infection,
- Incidence of adverse events over the time course of the trial (pre, during and post pandemic),
- Incidence of adverse by country or analysis region, age and gender over the time course of the trial (pre, during and post pandemic)

17.2. LABORATORY EVALUATIONS

A urine pregnancy test will be conducted as needed for women of childbearing potential. Pregnancy test results will be presented in a data listing.

18. DATA NOT SUMMARIZED OR PRESENTED

The other variables and/or domains not summarized or presented are:

- Comments

These domains and/or variables will not be summarized or presented, but will be available in the clinical study database, SDTM and/or ADaM datasets.

19. REFERENCES

Clopper CJ, Pearson ES. The use of confidential or fiducial limits illustrated in the case of the binomial. Biometrika 1934; 26:404-413.

Miettinen O., Nurminen M. Comparative analysis of 2 rates. *Statistics in Medicine* 1985; 4(2):213-26

Nauta J. Statistics in Clinical Vaccine Trials. 2010. Heidelberg: Springer.

U.S. Department of Health and Human Services, Food and Drug Administration, CDER/CBER (2016): Guidance for Industry Non-Inferiority Clinical Trials to Establish Effectiveness

ICH Harmonized Guideline for Estimands and Sensitivity Analysis in Clinical Trials E9 (R1). 2017.

APPENDIX 1. PROGRAMMING CONVENTIONS FOR OUTPUTS

IQVIA Output Conventions

Outputs will be presented according to the IQVIA output conventions.

Document Headers

All TFL is to include the following header:

GSK Vaccines Vaccine: MenABCWY Study 213171 (MenABCWY-19) - *DELIVERY DESIGNATION*

where delivery designation is the name of the current delivery, e.g., DRY-RUN, FINAL REPORT, etc.

Dates & Times

Depending on data available, dates and times will take the form yyyy-mm-ddThh:mm:ss.

Spelling Format

English US.

Presentation of Vaccine Groups

For outputs, vaccine groups will be represented as follows and in the given order:

Vaccine Group	For Tables, Listings and Figures
ABCWY	ABCWY + Placebo
ACWY	ACWY + Men B

Presentation of Visits

For outputs, visits will be represented as follows and in that order:

Long Name (default)	**Short Name**
Baseline	BL
Day 1, Month 0 (Visit 1)	D1 (M0)
Day 31, Month 1 (Visit 2)	D31 (M1)
Day 181, Month 6 (Visit 3)	D181 (M6)
Day 211, Month 7 (Visit 4)	D211 (M7)
End of Study	EoS

Tables

The 'Missing' category, when appropriate, will only be presented if participants qualify for this category. Otherwise, the row for 'Missing' will not be presented.

Decimal places

Decimal places for percentages and their corresponding confidence limits will be displayed with:

Percentages and their corresponding confidence limits will be displayed with:

- no decimals when there are fewer than 50 participants in each tabulated group
- one decimal when there are at least 50 participants in at least one tabulated group
    - Exceptions will be made for percentages that are not 0% or 100% but appear as 0% or 100% due to rounding. For these specific cases the number of decimals will be increased until the displayed value is no longer 0% or 100%. Examples are given in the following table.

n/N	Displayed percentage
10/45	22%
1/45	2%
10/55	18.2%
1/55	1.8%
1/300	0.3%
1/3000	0.03%
1/30000	0.003%
299/300	99.7%
2999/3000	99.97%
29999/30000	99.997%

- The display of additional decimals for values close to 0% or 100% will be applied only to point estimates and not confidence limits, which can be rounded and displayed as 0% or 100%.
- Values of exactly 0% or 100% will be presented with no decimals regardless of the number of participants per tabulated group.
- Differences in percentages and their corresponding confidence limits will be displayed with one more decimal than the maximum number used to display the individual percentages, for example the difference between two percentages displayed with one decimal will be displayed with two decimals.

Decimal places for Demographic and baseline characteristics will be as follows:

- The mean, median, and standard deviation for continuous baseline characteristics (height, weight, body mass index (BMI), pre-vaccination body temperature) will be presented with one decimal.
- The minimum and maximum values and quartile values (if required) will be presented with the same number of decimals as the observed values.
- The maxima and minima of transformed height variables will be displayed with no decimals.
- The maxima and minima of transformed weight variables will be displayed with no decimals

with the exception of values are below 10kg where one decimal will be displayed.

- The maximum and minima of transformed body temperatures will be displayed with one decimal.

Serological Summary Statistics

The number of decimals used when displaying geometric mean titers (GMT) or concentrations (GMC) and their confidence limits is shown in the following table:

GMT or GMC value	Number of decimals to display
<0.1	3
>=0.1 and <10	2
>=10 and <1000	1
>=1000	0

When multiple categories of GMT or GMC values are present in the same table, the number of decimals displayed should match that of the smallest category (i.e. the one with the higher number of decimals). For example, if GMT or GMC values of <0.1 appear in the same table as values of >=0.1 and <10, 3 decimals should be displayed for both.
GMT or GMC ratios and their confidence limits will be displayed with 2 decimals regardless of the actual values.

Data Listings

All data listings will be ordered by the following (unless otherwise indicated in the template):

- Randomized vaccine group (or intervention received if it's a safety output),
- Center-participant ID,
- Date (where applicable),
- For data listings where non-randomized participants would be included, these will appear in a category after the randomized vaccine groups labeled 'Not Randomized'.

File Naming Convention

The output files and corresponding SAS programs will have the same name.

The filename will start with 't', 'l' or 'f', respectively for table, listing or figure.

The filename will end with a brief description of the output content.

For output filenames (and corresponding SAS programs) that include numbers, include leading zeroes ('0') when the number is smaller than 10.

Elements in the file name will be separated by underscores '_'.

APPENDIX 2. PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the data listings.

When partially completed dates (i.e. with missing day or month) are used in calculations, the following standard rules will be applied:

- A missing day will be replaced by 15
- A missing day and month will be replaced by June 30th.

The following exceptions apply:

- Imputed adverse event end date occuring before the actual start date
  - If the imputed event end date occurs before the event start date then the imputed end date will be December 31st, unless this occurs after the study conclusion date in which case the earlier date is used.
- Adverse event start dates with missing day:
  - If the event starts in the same month as at least one of the study doses, the contents of AE.AESTRTPT (the flag indicating if the event occurred before or after vaccination) will be used to complete the date. If 'after vaccination' is selected, the imputed start date will match the first (or only) study dose given during that month. If 'before vaccination' is selected, the imputed date will be one day before the first (or only) study dose given during that month.
- Adverse event start dates with missing day and month:
  - If the event starts in the same year as at least one of the study doses, the contents of AE.AESTRTPT (the flag indicating if the event occurred before or after vaccination) will be used to complete the date. If 'after vaccination' is selected, the imputed start date will match the first (or only) study dose given during that year. If 'before vaccination' is selected, the imputed date will be one day before the first (or only) study dose given during that year.

- Adverse event start dates with missing day and month:

All other cases of incomplete AE or concomitant medication/vaccination start date will follow the standard rules above.

APPENDIX 3. PROTOCOL DEVIATIONS AND EXCLUSIONS FROM ANALYSIS SETS

Details of exclusions from each analysis sets are provided below. A complete list of participants excluded from each analysis set will be reviewed and confirmed by the sponsor prior to unblinding.

Exclusion from Exposed Set (ES)

'Study intervention not administered at all', 'Fraudulent data' and code 'Invalid informed consent or fraudulent data' will be used for identifying participants excluded from ES.

Exclusion from unsolicited and solicited safety set

Unsolicited safety set

'Study intervention not administered at all', 'fraudulent data', 'invalid informed consent' and 'no post-dose safety data' will be used for identifying participants excluded from the unsolicited safety set.

Solicited safety set

'Study intervention not administered at all', 'fraudulent data' and 'invalid informed consent' and 'no post-dose solicited safety data' will be used for identifying participants excluded from the solicited safety set.

Exclusion from Full Analysis Set (FAS)

'Study intervention not administered at all', missing laboratory (Immunology) assessment (missed visit, blood draw not done at visit, sample not available for testing, result not available) and 'Fraudulent data' will be used for identifying participants excluded from the FAS.

Exclusion from Per-protocol analysis Set (PPS)

A participant will be excluded from the PPS Immunogenicity analysis under the conditions presented in Table 3:

Table 3: Protocol deviations mapping and exclusion from analysis sets

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
1. Informed Consent Criteria	1A - Signed informed consent/assent not available on site	All
	1B - Wrong informed consent/assent version signed	All
	1C - Informed consent/assent not signed and/or dated by participant (parent/Legal rep)	All

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
	1D – Informed consent/assent not signed and/or dated by appropriate site staff	
	1E - Informed consent/assent not signed prior to any study procedure	All
	1OT - Other informed consent/assent deviations	All Manual case-by-case review
	3A - Not withdrawn from study after developing withdrawal criteria	All Manual case-by-case review
2. Eligibility and Entry Criteria	2 - Eligibility criteria not met	All
	7A - Study treatment not administered per protocol	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7B - Study treatment administered while contraindication	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively) Manual case-by-case review
	8A - Randomization procedure (subj assigned to wrong treatment, subj rand out of order)	All

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
3. Concomitant Medication Criteria	4A - Medication, excluded by the protocol, was administered	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	4B - Vaccine, excluded by the protocol, was administered	By visit for Day 31 and Day 211** (based on treatment administered on Day 1 and Day 181 respectively).
4. Laboratory Assessment Criteria	8G - Biological sample specimen procedures	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6A - Missed assessment* **when impacting lab samples*	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6D - Out of Window assessment* **when impacting lab samples*	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
5. Study Procedures Criteria	3A - Not withdrawn from study after developing withdrawal criteria	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
	3B – Not discontinued from study treatment	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6A - Missed assessment	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6B – Incomplete assessment	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6C – Assessment not properly performed	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6D - Out of Window assessment	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	6OT - Other assessment or time point window	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7B – Study treatment administered while contraindication	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
	8C – Non study treatment supply procedures	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	8D – eDiary procedures	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	8F – Post study treatment observation not done	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	8OT - Other deviation from study procedures	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively) Manual case-by-case review
6. Serious adverse event criteria	9B – Adverse event of special interest	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	9C - Pregnancy	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	9E – SAE not reported within the expected time frame	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	9F – Failure to confirm causality assessment within the expected time frame	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
	9OT – Other	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
7. Randomization Criteria	8A - Randomization procedure (subj assigned to wrong treatment, subj rand out of order)	All
	8B - Study blinding/unblinding procedures	By visit for Day 31 and Day 211** (based on treatment administered on Day 1 and Day 181 respectively). Manual case-by-case review
8. Visit Schedule Criteria	5A – Missed visit/phone contact	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	5B – Out of window visit / contact	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
9. Investigation Product (IP) Compliance	7A - Study treatment not administered per protocol	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7C - Wrong study treatment or assignment administered	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
	7D - Expired study treatment administered	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7E - Use of study TRT impacted by temperature excursion - not reported/approved/dispensed	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7F - Study treatment not prepared as per protocol (e.g. reconstitution)	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7G - Study treatment not available at site for administration	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7H- incorrect volume given	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7OT - Other deviations related to wrong study treatment/administration/dose (study treatment not available at site for administration, Commercial Vx used in place of study Vx, study treatment administered while contraindication)	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively) Manual case-by-case review
	6G - Out of Window - Treatment administration	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
10. Efficacy Criteria	3A - Not withdrawn from study after developing withdrawal criteria	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively)
	7B - Study treatment administered while contraindication	By visit for Day 31 and Day 211 (based on treatment administered on Day 1 and Day 181 respectively) Manual case-by-case review
11. Administrative Criteria	8E – Equipment procedures	All
12. Source Document Criteria	8B – Study blinding/unblinding procedures	All
13. Regulatory or Ethics Approvals Criteria	8OT – Other deviation from study procedures	All
14. Other Criteria To be discussed on a case-by-case basis	7OT – Other deviations related to wrong study treatment/administration/dose	All
	8E – Equipment procedures	All
	8OT – Other deviations from study procedure	All
	10A- Fraudulent data	All

CTMS * Categories	GSK Deviations Code/ Description	Visit (timepoints) where the exclusion is applicable
	10B-Any other GCP non-compliance	All Manual case-by-case review

* CTMS = Clinical Trial Management System. Additional details can be found in PDMP.

** All visits that follow when the exclusion occurs are also excluded.

Note: The '4. Laboratory Assessment Criteria' includes blood draws (immunogenicity) and the '5. Study Procedures Criteria' includes the vaccination procedures.

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Certificate Of Completion

Envelope Id: BCEFB67708CC49FABFECE6E724D3E561
Status: Completed
Subject: Please DocuSign: MENABCWY(213171)_SAP_Amend4-Final_05SEP2022.docx
Project Code (Enter 0 for non-billable projects): QZA97505
IQVIA ID (Login ID): PPD
Business Unit:
Global Business Operations
Source Envelope:
Document Pages: 68
Signatures: 4
Envelope Originator:
Certificate Pages: 5
Initials: 0
PPD
AutoNav: Enabled
One IMS Way
EnvelopeId Stamping: Disabled
Plymouth Meeting, 19462
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PPD

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Status: Original
9/7/2022 4:22:08 AM
Holder: PPD
Location: DocuSign

Signer Events	Signature	Timestamp
PPD Security Level: Email, Account Authentication (Required)	PPD With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 9/7/2022 4:25:09 AM Viewed: 9/7/2022 4:25:45 AM Signed: 9/7/2022 4:26:04 AM
Electronic Record and Signature Disclosure: PPD Security Level: Email, Account Authentication (Required)	PPD With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 9/7/2022 4:25:10 AM Viewed: 9/7/2022 9:09:02 AM Signed: 9/7/2022 9:09:40 AM
Electronic Record and Signature Disclosure: PPD		

Signer Events	Signature	Timestamp
PPD Security Level: Email, Account Authentication (Required)	PPD With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 9/7/2022 4:25:10 AM Viewed: 9/15/2022 1:46:04 AM Signed: 9/15/2022 1:46:27 AM
Electronic Record and Signature Disclosure: PPD		
PPD Security Level: Email, Account Authentication (Required)	PPD With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 9/7/2022 4:25:10 AM Viewed: 9/7/2022 4:29:14 AM Signed: 9/7/2022 4:34:01 AM
Electronic Record and Signature Disclosure: PPD		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	9/7/2022 4:25:10 AM
Certified Delivered	Security Checked	9/7/2022 4:29:14 AM
Signing Complete	Security Checked	9/7/2022 4:34:01 AM
Completed	Security Checked	9/15/2022 1:46:27 AM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

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Browsers:	• Internet Explorer (Windows Only) 8.0 or above – compatibility mode is supported only for 9.0 and above. • Windows Edge Current Version • Mozilla Firefox Current Version • Safari (Mac OS only) 6.2 or above • Google Chrome Current Version
PDF Reader:	Acrobat® or similar software may be required to view and print PDF files
Screen Resolution:	1024 x 768 Recommended
Enabled Security Settings:	Allow per session cookies
Mobile Signing:	• Apple iOS 7.0 or above • Android 4.0 or above

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